WHO Target Product Profiles for COVID-19 Vaccines
Revised version, April 2022

Purpose of the document

Selected disease areas are identified as WHO priorities for research and product development. In the case of COVID-19, target product profile development followed the COVID-19 Global research and innovation forum: towards a research roadmap[1]. This target product profile[2] is intended to convey, based on the most recently available data, WHO's current priorities for vaccine development, regardless of regimen (including whether they are intended as primary vaccination or as boosters), and whether they are intended to address currently circulating variants or future variants.

The target audience includes vaccine scientists, product developers, manufacturers and funding agencies.
All the requirements contained in WHO guidelines for WHO policy recommendation and prequalification will also apply. The criteria below lay out some of the considerations that will be relevant in WHO's case-by-case assessments of COVID-19 vaccines in the future. Therefore, should a vaccine's profile be sufficiently superior to the critical characteristics under one or more categories, this may outweigh failure to meet another specific critical characteristic. Vaccines which fail to meet multiple critical characteristics are unlikely to achieve favorable outcomes from WHO's processes. Modelling of the potential impact of COVID-19 vaccines with different efficacy profiles, administered using different immunization strategies, at different stages of the epidemic is a high priority to further refine desired characteristics. For certain vaccine characteristics, additional footnotes are provided on the rationale and assumptions made.

Acknowledgement

WHO gratefully acknowledges the R&D Blueprint Working Group on Target Product Profiles for COVID-19 vaccines[3] and the many individuals and institutions that provided comments to the draft at the public consultation stage.

[1] https://www.who.int/publications/m/item/a-coordinated-global-research-roadmap
[2] https://www.who.int/blueprint/priority-diseases/key-action/WHO_Target_Product_Profiles_for_COVID-19_web.pdf

[3] https://www.who.int/publications/m/item/who-working-group-target-product-profiles-for-covid-19-vaccines

I. Background

On April, 2020, WHO released its initial Target Product Profile for COVID vaccines, to help inform the development of these vaccines. Now that vaccines are available and there is more information both about feasibility and likely use of vaccines, as well as potential limitations posed by variants, the TPP is being revised to reflect more current information.

Roadmap strategic goal: Develop and make vaccines available under Emergency Use Listing and ultimately pre-qualification that will protect people around the world from adverse health consequences caused by COVID-19, particularly severe disease and death. Key attributes of vaccines include safety, efficacy (including durability and robustness to viral evolution), and deployability (including stability, availability around the world and potential for scale-up).

As before, this document describes the preferred and minimally acceptable profiles for human vaccines for COVID-19. All vaccines considered for use must meet appropriate regulatory standards. In general, the minimally acceptable profiles are aligned with expectations for emergency use listing of new vaccines. Licensed or pre-qualified vaccines would likely have more of the attributes of the preferred profile.

This revised Target Product Profile (TPP) was developed through a consultation process with key stakeholders in human and animal health, scientific, funding and manufacturing communities. It is intended that it will guide and prioritize the development of vaccines and decisions about need for boosters, based on the available data on COVID-19 and circulating variants of concern. As new scientific evidence is generated, this TPP may again require further review and revision.

Vaccine characteristic	Preferred	Critical or Minimal[4]
Indication for use	For immunization to prevent severe disease and death caused by COVID-19[5] . Activity against other coronaviruses (including other sarbecoviruses) and/ or potential future variants is highly preferred.	For immunization to prevent severe disease and death caused by COVID-19
Contraindication	Minor (e.g. hypersensitivity or conditions linked to specific adverse events)	Some contraindications may be acceptable
Target population	Adults, including elderly and others at risk of severe disease. Pediatrics (with appropriate dosing). Data should support administration to important groups[6]	Adults, including elderly and others at risk of severe disease
Safety/Reactogenicity	Substantial evidence of safety and efficacy, sufficient to support a highly favourable benefit/risk[7] profile.	Safety and reactogenicity whereby vaccine benefits outweigh safety risks.

[4] Generally aligned with Emergency Use Authorization Listing of Vaccines

[5] Prevention of mild disease predicts protection against severe disease

[6] Important groups include pregnant and lactating women, the immunocompromised.

[7] Benefit/risk may depend on age and other factors, including those predisposing to more severe covid or to greater incidence of adverse events. Benefit/risk assessment should take potential for enhanced disease into account. Benefit/risk assessment may change as information becomes available about rare adverse events.

Vaccine characteristic	Preferred	Critical or Minimal[4]
Measures of Efficacy	<u>For initial vaccination series:</u> Efficacy[8] against symptomatic disease with ~70% point estimate and lower 95% confidence interval ≥50% OR Efficacy against severe disease[9,10] with 90% point estimate and 70% lower bound. <u>For booster doses (doses after primary series):</u> Additional or booster doses (whether of the same or different vaccines) should be considered when vaccines no longer meet or appear to meet the severe disease criterion, and additional/booster doses must reach the severe disease criterion Vaccines with efficacy against transmission are preferred. <u>For previously infected:</u> Evidence of >70% effectiveness against severe disease.	<u>For initial vaccination series:</u> Efficacy against symptomatic disease with ~50% point estimate and lower 95% confidence interval ≥30% OR Efficacy against severe disease with 70%-80% point estimate and 30% lower bound[11]. <u>For booster doses (doses after primary schedule):</u> Additional or booster doses (whether of the same or different vaccines) should be considered when vaccines no longer meet or appear to meet the severe disease criterion, and additional/booster doses must reach the severe disease criterion

[8] Efficacy or Effectiveness, which should be assessed against currently circulating variants of concern.
[9] Severe disease endpoints may include long COVID, but are not required to.
[10] Immunobridging, based on standardized and validated assays, and with appropriate regulatory concurrence, can be used to predict that vaccines will meet specific efficacy criteria.
[11] Lower bound may be 0% if vaccine meets criteria for efficacy against symptomatic disease

Vaccine characteristic	Preferred	Critical or Minimal[4]
Dose regimen	Single- or two-dose primary series[12]. Ability to use vaccine as part of a heterologous regimen	Two-dose regimen[13]
Durability of protection	Confers protection against severe disease for at least 1 year in healthy adults and children. Lower frequency (Yearly or less frequently) of booster doses is preferred[14]	Regimens requiring booster doses in order to retain protection against severe disease are permitted Durability data is not required, but immunogenicity data to support likely duration of protection is desirable.
Deployability		
Route of Administration	Non-parenteral (syringe/needle or other adjunct equipment-avoiding) is preferred for ease of rapid administration and other logistical issues.	Any typically used route of administration is acceptable, if vaccine is safe and effective.
Product Stability and Storage	Higher storage temperatures and higher thermostability (e.g., longer storage at refrigerator temperatures) supported by relevant VVM type on the primary container (e.g., temperature indicator VVMs). Demonstration of at least 2-month stability at 2-8°C. No freeze sensitivity/potential damage	Minimum storage condition of -20 to -25 °C for longer-term storage. Demonstration of at least 30 days stability at 2-8°C and several hours stability at 25-30°C
Co-administration with other vaccines	Potential for coadministration with other vaccines (e.g., flu, polio, measles, pneumococcal) preferred	Stand-alone administration is acceptable

[12] Note strong preference for single-dose, but do not desire to discourage development of 2-dose vaccines if that is what is feasible.
[13] Many 2 dose vaccines confer partial protection after a single dose. For two-dose vaccines, protection after single dose should be assessed.
[14] Data likely to be obtained from real-world studies

Vaccine characteristic	Preferred	Critical or Minimal[4]
Presentation	Multi-dose presentation[15] is preferred for ease of use in campaigns. Lack of need for reconstitution. Barcodes on secondary packaging. Including serialization, GTIN, expiry and lot number. For parenteral, dose volume of 0.5 mL preferred, with AD syringes that are WHO prequalified.	Multi- or mono- dose presentations are acceptable.[16] .
Registration and Prequalification	Meets criteria for WHO pre-qualification[17,18]:	Meets criteria for WHO EUL[19]
Availability	Capability and firm developer commitment to make vaccine available to LMICs (as in minimal criteria) on an acceptable timeline, either directly or via technology transfer. (Platform) technologies that allow rapid scale up as well as shifting to next vaccine version (e.g. against future virus variants)	Capability to rapidly scale-up production[20] at cost/dose that allows broad use of selected regimen, including in LMIC, with availability of sufficient doses at cost/dose that allows broad use, including in LMICs. Where additional supplies are needed, these supplies are readily available.

[15] Multi-dose presentations should be formulated, managed and discarded in compliance with WHO's multi-dose vial policy. If feasible, vaccines consistent with an "open vial" policy may have additional advantages

[16] On 24 May the following text was removed from the critical or minimal characteristics: **Barcodes on secondary packaging. Including serialization, GTIN, expiry and lot number**.

[17] Prequalification process is described at: http://apps.who.int/medicinedocs/documents/s21095en/s21095en.pdf. https://apps.who.int/iris/bitstream/handle/10665/148168/WHO_IVB_14.10_eng.pdf

[18] Programmatic suitability considerations for pre-qualified vaccines are described at: http://apps.who.int/iris/bitstream/10665/76537/1/WHO_IVB_12.10_eng.pdf

[19] EUL considerations are described at: https://extranet.who.int/pqweb/vaccines/covid-19-vaccines

[20] Includes ancillary supplies, e.g., syringes, diluent, etc.